

Application No.: 10/526,692
Filing Date: August 4, 2005

REMARKS

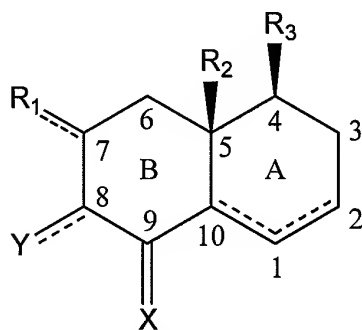
Claims 26, 27, 29-31, 33-36, 38-41, 44-57 and 79 are pending. Claims 33-36 and 38-40 are withdrawn as they relate to a non-elected invention. Claims 26, 27, 29-31, 41, 44-57 and 79 have been examined. The claims have been amended to reflect the specific stereochemistry of the compounds of the present invention at positions 4, 5 and where there is a single bond to R₁ at the 7 position. The compounds of the present invention are related to eremophilone compounds isolated from *Eremophila mitchelli* and encompass compounds such as eremophilone (EM-1), for which support is found in the Specification as filed, for example at page 11, last line, and in Example 1 at page 37). No new matter has been added herewith. The following addresses the substance of the Office Action.

Obviousness

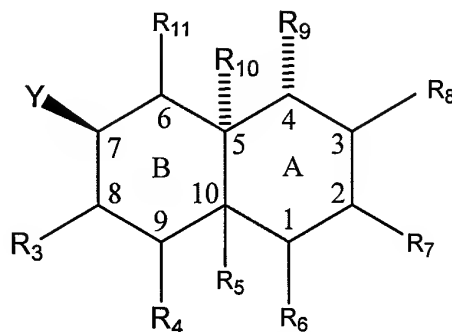
Claims 26, 27, 29-31, 41, 44-57 and 79 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Maupin et al. (WO 02/50053) in view of Chetty et al. (1969 *Tetrahedron Letters* 5:307-309) as evidenced by Gonzales-Coloma et al. (1995 *J Chem Ecology* 21:1255-1270). Maupin et al. discloses pesticidal sesquiterpenes, which include eremophilone, and Chetty et al. discloses 7a(H)-Eremophila-1,11-dien-9-one. Evidence of antifeedant activity by sesquiterpenes is disclosed by Gonzalez-Coloma et al. Thus, the Examiner concluded that it would have been obvious to combine the cited references and arrive at the claimed methods.

The Applicants wish to point out that a very large number of compounds are encompassed by formula (I) of Maupin et al.. The compounds include those of formula (III) described at page 20 and these compounds broadly include the eremophilone compounds of the present invention. Each of formulas (I) and (III) of Maupin et al. include a general fused bicyclic ring structure that may be substituted in any or all positions available. However, the compounds exemplified and tested are all nootkatone and valencene sesquiterpenes isolated from the Alaskan Yellow Cedar.

The compounds of the present invention and in Maupin et al. are as follows, with corresponding carbon atoms on the rings numbered 1-10:



Present invention



Maupin et al.

However, the compounds of Maupin et al., which are disclosed as having pesticidal activity against fleas, ticks and mosquitoes, differ from those of the present invention in at least the following five particularly important ways.

1. For the compounds of the presently claimed methods, when ----- is a single bond, the compounds have substituents R₁, R₂ and R₃ in a syn arrangement (i.e., all are on the same face of the molecule). In contrast the same substituents in the Maupin et al. compounds, i.e., R₉, R₁₀ and Y have R₉ and R₁₀ syn to one another on the same face of the molecule, and Y anti relative to R₉ and R₁₀ (i.e., on the opposite face of the molecule).

2. The compounds of the present invention have a carbonyl group or carbonyl derivative in the 9-position. In contrast, none of the compounds exemplified in Maupin et al. have any substitution in the 9-position (R₄).

3. The compounds of the present invention have optional substitution in the 8-position. In contrast, none of the exemplified compounds of Maupin have substitution in the 8-position (R₃).

4. The compounds of the present invention do not have substitution in the A ring other than in the 4-position. In contrast, many of the compounds exemplified in Maupin have substitution on the A ring, especially in the 2-position (R₇).

5. The compounds of the present invention may have a double bond linking R₁ to the fused bicyclic ring. In contrast, in the compounds described by Maupin, Y is not linked to the C₇ carbon by a double bond.

Chetty et al. describes the isolation of eremophilone compounds of the present invention from *Eremophila mitchelli*. However, the reference merely describes the isolation of the compounds and their structure. There is no teaching or suggestion of their biological activity and, based on Chetty et al., one of ordinary skill in the art would have had no reason to believe that the compounds could be pesticidal, particularly against wood associated pests such as termites.

Although the broad disclosure of Maupin et al. may encompass the compounds of the present invention, there is no specific disclosure of the claimed compounds having the stereochemistry as shown in the claims. Moreover, a person skilled in the art would realize that the compounds exemplified by Maupin et al. have a distinctly different three dimensional structure where the positions of the substituents are different and the shapes of the A and B rings are different from those of the present invention. Furthermore, it is well known in the chemical and biological fields that one enantiomer or diastereomer of a compound may have biological activity and the other enantiomer or another diastereomer may have none or very little activity. It is not possible to predict, before testing, which enantiomer or diastereomer will have biological activity. A person skilled in the art, in possession of Maupin et al. and Chetty et al., would not have considered the disclosure of Maupin et al. and believed with any reasonable expectation of success that the compounds disclosed by Chetty et al. would have the same activity.

The Examiner referred to Gonzalez-Coloma as evidence that sesquiterpenes have antifeedant activity. Gonzalez-Coloma refers to two very specific sesquiterpene compounds, 2,10-bisaboladien-1-one and 11 β -acetoxy-5-angeloyloxy-silphinen-3-one. The term "sesquiterpene" is a very broad term that encompasses terpenes that consist of three isoprene units and have a basic molecular formula C₁₅H₂₄. Sesquiterpenes may be monocyclic, bicyclic or tricyclic and have varied structures. 2,10-bisaboladien-1-one is a monocyclic sesquiterpene and 11 β -acetoxy-5-angeloyloxy-silphinen-3-one is a tricyclic sesquiterpene. Neither compound is a fused bicyclic sesquiterpene compound similar to the eremophilone compounds of the present invention. Moreover, it is not possible to conclude that all sesquiterpenes have insect antifeedant activity based on the disclosure that two specific sesquiterpenes have antifeedant activity against one species of beetle.

Attached is a Declaration by inventor Robert Spooner-Hart, which indicates that pesticidal activity, repellant activity and antifeedant activity are three distinct activities that do

not necessarily overlap. Furthermore, biological activity of sesquiterpenes in general and eremophilone compounds specifically cannot be predicted based on structure. The Applicants have shown that eremophilone compounds having a 9-oxo group and no substitution in the A ring in positions 1, 2 and 3 have pest controlling activity and the claims are directed to such compounds. This activity cannot be predicted from the combination of Maupin et al., Chetty et al., and Gonzalez-Coloma et al.

In view of the amendments to the Claims and the preceding remarks, the claims are non-obvious in light of Maupin et al., Chetty et al. and Gonzalez-Coloma et al. Accordingly, the Applicants respectfully request that the rejection be withdrawn.

Double Patenting

Claims 26, 27 and 29-31 were rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 13-16, 19-20, 32-33, 37 and 38 of U.S. Patent No. 7,129,271, in view of Chetty et al. (*supra*). However, as noted above, the present claims have been amended so that the substituents R₁, R₂, and R₃, when R₁ is attached to the ring through a single bond, are all syn to one another.

U.S. Patent No. 7,129,271 is the U.S. National Phase of Maupin et al. (WO 02/50053), as discussed above. Importantly, claims 1-11 in U.S. Patent No. 7,129,271 have been limited to compounds in which substituents R₉ and R₁₀ are syn to one another and substituent Y is anti to substituents R₉ and R₁₀. As discussed above, this is in contrast to the present invention in which the compounds have the substituents equivalent to R₉, R₁₀ and Y all in a syn arrangement on the same face of the molecule. Although the stereochemistry of the compounds in the method of claim 13 of U.S. Patent No. 7,129,271 is not defined, there is no teaching to use the compounds of the present invention where the substituents R₉, R₁₀ and Y are in a syn relationship with one another. In fact, U.S. Patent No. 7,129,271 teaches away from the stereochemistry claimed in the present application as the compounds claimed in claims 1-11 are limited by having a different stereochemical arrangement of substituents R₉, R₁₀ and Y.

Although Chetty et al. describes the isolation and structure of compounds of the present invention, there is no indication or teaching of any biological activity. A skilled artisan would not consider using eremophilone compounds in methods of controlling pests in light of U.S. Patent No. 7,129,271 in view of Chetty et al. with any reasonable expectation of success.

Application No.: 10/526,692
Filing Date: August 4, 2005

In view of the amendments to the claims and the preceding remarks, the Applicants respectfully request that the rejection on the ground of nonstatutory obviousness-type double patenting be withdrawn.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

In view of Applicants' amendments to the Claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Application No.: 10/526,692
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Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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